Recognizing Microcephaly and Other Presentations of Zika Virus Syndrome

AAP Series on Zika Virus Syndrome
Webinar for Clinicians #1
Tuesday, January 10, 2017 at 2:00 pm ET/1:00 pm CT
Disclosures

• The presenters have no relevant financial relationships with the manufacturers(s) of any commercial product(s) and/or provider of commercial services discussed in this activity.

• The presenters do not intend to discuss an unapproved/investigative use of a commercial product/device in this presentation.
OBJECTIVES

1. Provide an overview of the neurodevelopmental manifestations of congenital Zika virus syndrome.
2. Describe how to monitor symptomatic and asymptomatic infants.
3. Discuss how to collaborate with specialists to ensure a continuum of care.
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Zika Virus: The Current Situation

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Chief Medical Officer,
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ZIKA CASES REPORTED IN THE UNITED STATES

LABORATORY-CONFIRMED ZIKA VIRUS DISEASE CASES REPORTED TO ARBONET BY STATE OR TERRITORY (AS OF DECEMBER 28, 2016)

Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection

<table>
<thead>
<tr>
<th>US States and the District of Columbia</th>
<th>US Territories</th>
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<tbody>
<tr>
<td>1,246</td>
<td>2,701</td>
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As of December 13, 2016

# Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States, 2016

As of December 13, 2016

<table>
<thead>
<tr>
<th>Completed pregnancies with or without birth defects</th>
<th>875</th>
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<tbody>
<tr>
<td>Liveborn infants with birth defects</td>
<td>34</td>
</tr>
<tr>
<td>Pregnancy losses with birth defects</td>
<td>5</td>
</tr>
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Top 3 Questions

Source: CDC’s pediatric inquiry hotline data
ROLE OF THE PEDIATRICIAN

• Share information; respond to questions
• Handle testing of patients.
• Update infant records in the US CDC Zika Pregnancy Registry.
• Support care coordination; ensure quality care within a medical home.
SELECT RESOURCES

**CDC RESOURCES:**
Pocket Guide

Guidance

**AAP RESOURCES:**
Zika Resource page
www.aap.org/zika

Key Zika Virus Information for Pediatricians

AAP Zika Information for Families
www.healthychildren.org/zika
The Impact of Congenital Zika Virus Infection on the Developing Nervous System

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OBJECTIVES

• Understand the impact of Zika Virus on the Developing Human Brain.
• Identify Congenital Zika Virus Syndrome and congenital microcephaly.
• Identify other manifestations of congenital Zika virus infection.
MECHANISMS OF *IN UTERO* ZIKV-ASSOCIATED BRAIN ABNORMALITIES

1. Disruption of Brain Development
   - Direct Viral Invasion of Neural Progenitor Cells in Early Pregnancy
   - Impaired or disrupted neuronal proliferation, migration & differentiation

AND/OR

2. Damage of Previously Developed Brain
   - Direct Viral Invasion & Destruction of Brain Cells
   - Possible Additional Immunologic Mechanisms


Congenital Zika Syndrome

- Recently recognized pattern of congenital anomalies associated with Zika virus infection during pregnancy that includes:
  - Severe microcephaly (small head size) resulting in a partially collapsed skull
  - Thin cerebral cortices with subcortical calcification
  - Macular scarring and focal pigmentary retinal mottling
  - Congenital contractures
  - Marked early hypertonia and symptoms of extrapyramidal involvement

Moore, CM., et al., Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. JAMA Pediatrics, 2016 Nov 3. (epub ahead of print)
Figure Legend:

Cranial Morphology Supporting **Fetal Brain Disruption Sequence** Phenotype in Congenital Zika Syndrome

A, Lateral view of an infant with congenital Zika virus infection. Note the severe decrease in cranial vault, irregularity of the skull, and scalp rugae. B, Typical scalp folds or rugae in a 3-month-old infant with presumed congenital Zika virus infection. C, Lateral skull radiograph in a newborn showing partial collapse of the cranial bones with prominent occiput. D, Fetal magnetic resonance image (MRI) showing same phenotype at 29 weeks’ gestation. The white arrowhead indicates occipital area. E and F, 3-Dimensional skull reconstruction in a 3-month-old infant showing downward displacement of the frontal and parietal bones while the occipital bone appears stable.

Brazilian ZIKV Causes Birth Defects in SJL Mice

Histopathological aspect of the cortical organization (brackets) in infected brains, including intranuclear vacuoles, and ‘empty’ nuclei aspect with chromatin margination in neurons (arrowheads).

Comment: Disruption of normal cortical layers in motor cortex and temporal lobes—evidence of abnormal migration.

Zika Virus Disrupts Development of the Human Fetal Brain

doi: 10.1148/radiol.2016161584
ZIKV-associated brain malformations

ZIKV-associated brain malformations

ZIKV-associated Arthrogryposis

doi: 10.1148/radiol.2016161584

Congenital ZIKV-Associated Eye Abnormalities

**Predicted Neurological Manifestations of Congenital ZIKV**

**Infants Abnormal at Birth**
(Most with Congenital Microcephaly)
- Profound Motor & Cognitive Impairment
  - Profound Intellectual Disability
  - Most will meet Dx criteria for CP
- Cortical Visual Impairment
- Cortical Auditory Impairment
- Oral-motor impairment
  - May worsen during first few months
  - Feeding problems & Aspiration
- High risk of seizures and epilepsy
  - Myoclonic seizures
  - Infantile Spasms

**Infants Who Appear Normal at Birth**
- Deceleration of Head Growth with “Acquired Microcephaly”
  - Less severely affected infants and children may retain normal head size
- Developmental Delay
  - One or more domains
  - Consistent with localization of lesion(s)
- High Risk of seizures and Epilepsy
  - Neonatal seizures
  - Myoclonic seizures & Infantile Spasms
- Onset of epilepsy later in childhood and adolescence.
  - Developmental regression may occur with onset of seizures


Guidance on Caring for Infants with Zika Virus Syndrome through Collaborations with Specialists and Monitoring Asymptomatic Infants

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OBJECTIVES

• Understand the role of the medical home in assuring coordinated care for children.
• Delineate the specialist needs of the infant with congenital Zika virus syndrome.
• Describe the medical home neighborhood concept as it relates to the care of infants with congenital Zika virus syndrome.
• Understand the recommendations for monitoring asymptomatic infants.
OBJECTIVES

• Understand the role of the medical home in assuring coordinated care for children.
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• Describe the medical home neighborhood concept as it relates to the care of infants with congenital Zika virus syndrome.
• Understand the recommendations for monitoring asymptomatic infants.
The Medical Home for Pediatric Primary Care

- Accessible
- Family-centered
- Continuous
- Comprehensive
- Coordinated
- Compassionate
- Culturally effective
THE MEDICAL HOME

• A usual source of care for sick and well-child care
• A personal doctor or a nurse
• Family-centered care
  • Trust
  • Made to feel like a partner in care
• No problems getting referrals
• Effective care coordination when needed
Medical Home as a Piece of a System of Care

• Access to a medical home
• Access to affordable insurance
• Family participation and satisfaction
• Early and continuous screening
• Easy to access community-based services
• Services necessary to transition to adulthood
System of Care Quality Indicators for Children Who are Severely Affected

- Family Partnership and Satisfaction
- Care in a Medical Home
- Adequate Insurance
- Early and Continuous Screening
- Services Organized for Ease of Use
- Effective Transition Planning
- Total System of Care
HEALTH SYSTEM GOAL FOR INFANTS WITH CONGENITAL ZIKA VIRUS SYNDROME

Family-centered and coordinated network of community based services that promote the health, development and well-being of children and their families

HEALTH SYSTEM GOAL FOR INFANTS WITH CONGENITAL ZIKA VIRUS SYNDROME

- Lack of communication
- Limited coordination
- Families feeling frustrated connecting the dots themselves
**Objectives**

- Understand the role of the medical home in assuring coordinated care for children.
- **Delineate the specialist needs of the infant with congenital Zika virus syndrome.**
- Describe the medical home neighborhood concept as it relates to the care of infants with congenital Zika virus syndrome.
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UPDATE: INTERIM GUIDANCE FOR THE EVALUATION AND MANAGEMENT OF INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION

Mother with laboratory evidence of Zika virus infection during pregnancy

Perform a comprehensive physical exam on infant, head ultrasound, standard newborn hearing assessment and infant Zika virus laboratory testing (Table 1)

Infant with findings consistent with congenital Zika syndrome

Initial evaluation (Box 2)

Infant without findings consistent with congenital Zika syndrome

Infant with laboratory confirmed or probable congenital Zika virus infection

Infant negative for congenital Zika virus infection

2 Pathways

Physical Exam & Head U/S

Findings consistent with congenital Zika virus syndrome

Normal newborn exam
REFERRALS FOR SPECIALISTS AND TESTING

- Child neurology
  - Imaging
  - Seizures (EEG)
  - Guide referral to neurosurgery if hydrocephalus requires shunting
- Pediatric Ophthalmologist
  - At birth & 3 months (includes retinal exam)
  - Retinal, optic nerve, abnormal vasculature, cataracts, lens subluxation, iris colobomas
- Audiologist
  - Auditory Brainstem Response (ABR) at birth and 4-6 months
  - May need behavioral audiology at 9 months
Referrals for Specialists and Testing

- Endocrinologist
  - Thyroid screen at 2 weeks and 3 months
  - Hypothalamic dysfunction leading to pituitary insufficiency
- Developmental Pediatrician and/or pediatric rehabilitation medicine physician
  - Write prescriptions for therapies, orthotics, equipment
  - Address irritability and sleep problems
- Orthopedic surgeon
  - To address arthrogryposis
- Pulmonologist and/or ENT
  - For airway management if aspiration is a problem
- Gastroenterologist
  - For inability to maintain nutritive status by mouth

**Other Referrals**

- **Palliative Care**
  - Irritability
  - Family goal setting
- **Family supportive services**
  - Respite
  - Psychological support
- **Lactation consultation, nutritionists, speech or occupational therapy**
  - Dysphagia
  - Risk of aspiration
- **Multidisciplinary clinic**
  - Cerebral Palsy and related disorders or
  - Complex care clinic
- **Early Intervention**
  - Physical therapy
    - Gross motor development
    - Range of motion
    - Splinting
  - Occupational therapy
    - Fine motor development
    - Range of motion
    - Splinting
    - Feeding and other activities of daily living
  - Speech and language pathology
    - Feeding and swallowing (swallow study)
    - Communication
  - Vision therapy
    - Stimulation
    - Magnification
    - Patching
OBJECTIVES

• Understand the role of the medical home in assuring coordinated care for children.

• Delineate the specialist needs of the infant with congenital Zika virus syndrome.

• Describe the medical home neighborhood concept as it relates to the care of infants with congenital Zika virus syndrome.

• Understand the recommendations for monitoring asymptomatic infants.
Health Neighborhood = Medical Home Neighborhood
Numerous Specialists → Care Coordination

- “A patient and family-centered, assessment driven, continuous team-based activity designed to meet the bio-psychosocial needs of children and youth while enhancing person and family caregiving skills and capabilities.”

- Care plan:
  - Based on shared goals
  - Includes medical summaries
  - Clarifies responsibilities
  - Delineates plans for action
Supplemental Security Income

Early Intervention

Family and friends for emotional support and help

Daycare for CSHCN


Tools

1. A Medical Home Neighborhood Mapping Template (Appendix G) can be copied, used and completed with children, families and their team.
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2 Pathways

Physical Exam & Head U/S

Findings consistent with congenital Zika virus syndrome

Normal newborn exam
MONITORING ASYMPTOMATIC INFANTS

- Provide care in a medical home
- Auditory brainstem response testing at one and 4-6 months
- Comprehensive ophthalmologic examination at one month
- Follow head circumference and other growth parameters
- Routine developmental screening with a validated tool at 9 months or earlier if any concerns exist
- Vision screening and visual regard testing at every visit
- Consider neuroimaging if concerned
ANTICIPATORY GUIDANCE

- Developmental milestones
- Lack of eye contact
- Abnormal tone
- Feeding and growth
- Irritability
- Abnormal movements
- Family support
  - Address fear and stress

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BOX 1. Areas of expertise and organizations represented at the Clinical Evaluation and Management of Infants with Congenital Zika Virus Infection meeting — Atlanta, Georgia, July 21–22, 2016

Specialties represented
Audiology
Clinical genetics
Critical care
Developmental and behavioral pediatrics
Endocrinology
Hospitalist medicine
Infectious disease
Lactation and infant feeding
Maternal-fetal medicine
Neonatology
Neurology
Nutrition
Ophthalmology
Orthopedics
Pediatrics
Physical medicine and rehabilitation

Partner organizations
American Academy of Family Physicians
American Academy of Pediatrics (including representation from the Puerto Rico chapter)
American College of Obstetricians and Gynecologists
Association of Maternal & Child Health Programs
Family Voices, Inc.
March of Dimes
National Association of Pediatric Nurse Practitioners
Parent to Parent of Georgia
Society for Maternal-Fetal Medicine

Federal agencies
Administration for Children and Families
CDC
Centers for Medicare & Medicaid Services
Maternal and Child Health Bureau, Health Resources and Services Administration
National Institute of Child Health and Human Development, National Institutes of Health
Office of the Assistant Secretary for Preparedness and Response
RESOURCES

- AAP Zika Virus (www.aap.org/zika)
- AAP Key Information for Pediatricians (www.aap.org/zikakey)
- CDC Zika Virus (www.cdc.gov/zika)
- ACOG Zika Virus Toolkit (http://www.acog.org/About-ACOG/ACOG-Departments/Toolkits-for-Health-Care-Providers/Zika-Toolkit)
Questions?

- Dial *1 on your phone to ask a live question.
- Phone: 844-216-1726
- Conference ID: 18985179

- You may also ask a question through the chat box in the lower left hand corner. The AAP staff or presenters will address unanswered questions via e-mail after the call.

- Please e-mail DisasterReady@aap.org to follow-up as needed.
THANK YOU!

Questions?

E-mail DisasterReady@aap.org